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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/065,456	10/19/2002	Toshio Kawai	020.0001	4033

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EXAMINER	
BABIC, CHRISTOPHER M	
ART UNIT	**PAPER NUMBER**
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/065,456	KAWAI, TOSHIO	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,6,7 and 9-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,6,7 and 9-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 28, 2007 has been entered. Claim(s) 4, 6, 7, and 9-12 are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claim(s) 4, 6, 7, and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haff et al. (EP 0 636 413 A2; February 1, 1995) in view of Onischenko (EP 0 504 435 A1; September 23, 1992).

With regard to claim(s) 4, Haff teaches methods for continuous DNA amplification (col. 3-7, for example. Specifically, Haff teaches an apparatus for continuous

amplification of DNA (fig. 1; col. 9-12, for example), comprising: a denaturing isothermal tank made up of a container body for holding a heat-exchange fluid (fig. 1; col. 10, lines 1-10, for example), a heating device for heating the heat-exchange fluid to (col. 11, Lines 50-55, for example), and retaining it at, a prescribed temperature for dissolving apart the DNA's double strands, and a stirring device for stirring the heat-exchange fluid (col. 10, lines 1-10, for example); an annealing isothermal tank made up of a container body for holding a heat-exchange fluid (fig. 1; col. 10, lines 1-10, for example), a heating device for heating the heat-exchange fluid to (col. 11, lines 50-55, for example), and retaining it at, a prescribed temperature at which primers contained in the reagent solution anneal to the DNA fragments, a stirring device for stirring the heat-exchange fluid (col. 10, lines 1-10, for example); an elongation isothermal tank made un of a container body for holding a heat-exchange fluid (fig. 1; col. 10, lines 1-10, for example), a heating device for heating the heat-exchange fluid to (col. 11, lines 50-55, for example), and retaining it at, a prescribed temperature at which complementary chains are extended continuously onto the primers, and a stirring device for stirring the heat-exchange fluid (col. 10, lines 1-10, for example). It is noted that fig. 1 discloses only two temperature zones, however, Haff teaches that three temperature stable liquid baths may be used for three separate incubation temperatures (col. 9, lines 30-40, for example).

Haff further teaches a circulation-path system through which the reaction mixture in the reaction-mixture tank is fed and guided, the circulation-path system being arranged such that it circuits from the reaction-mixture tank and goes by way of the

denaturing, annealing, and elongation isothermal tanks (fig. 1; col. 10, lines 25-45, for example); and a pump working to feed the reaction mixture in said circulation-path system unidirectionally through it (fig. 1; col. 15-30, for example); wherein the apparatus is configured such that the reaction mixture in said circulation-path system is for timed intervals maintained at prescribed temperatures determined by the heat-exchange fluids in the isothermal tanks (col. 12, lines 1-20, for example); and connected by intervening out-of-tank sections (figure 1, 2B, for example).

It is noted that the use of the term "tank" does not patentably distinguish the present invention from the teachings of Haff even though the present invention appears to be a large-scale amplification apparatus, because term is not defined within in the specification in any manner that would indicate a required volume capacity of the apparatus, i.e. the term is not defined in any manner within the specification or claim language itself that would require reaction volumes thought to be of a large-scale nature. Furthermore, Haff teaches that the fig. 1 embodiment can perform PCR on a reaction volume of ANY scale (col. 9, lines 15-30, for example).

With regard to claim(s) 6, Haff teaches a heating device containing a pump for circuit-feeding the heat-exchange fluid in between the container body and the heating device, and a heat source for heating the heat-exchange fluid to and retaining it at prescribed temperatures, wherein said heating device supplies the heat-exchange fluid to said container body (fig. 3; col. 14-16). A practitioner of ordinary skill in the art would have recognized that the heating elements above could have been incorporated into the apparatus disclosed in fig. 1 of Haff et al.

With regard to claim(s) 7 and 9, Haff teaches a *single* continuous reaction tube passing through temperature zones (fig. 1; col. 10, Lines 25-45, for example) and a series of parallel tubes for greater control of reaction parameters (figure 5; col. 16-19, for example).

With regard to claim(s) 10-12, Haff teaches that additional baths could be added to increase the number of incubation temperatures (col. 4, Lines 5-10, for example).

Haff does not expressly teach a coiled heat-exchange section immersed in to the reaction sections of fig. 1, however, Haff does teach a looped capillary tubing wherein the number of loops is directly related to the number of cycles (i.e. time of total amplification reaction) (col. 13 and 14). Thus, Haff teaches that "looping" the reaction tube can control the period of time a reaction mixture is a certain temperature or series of temperatures. Furthermore, they disclose that the length of tubing is directly related to the residence time of the reaction mixture in each temperature zone, expressly highlighting that tubing of greater length is preferred to achieve better temperature control (col. 10, for example).

Thus, it would have been further *prima facie obvious* to a practitioner of ordinary skill in the art at the time of invention a coiled heat-exchange section immersed into the tubing of the apparatus of Haff since Haff suggests such a modification to control residence time of the reaction mixture in each temperature zone.

Haff does not expressly *teach* recirculating the *same* amplification reaction mixture through *three* temperature zones by the way of a single path and reaction mixture tank as required by the current invention. Haff expressly teaches that the *same*

reaction mixture is cycled through the temperature zones of the apparatus in fig. 1, however, Haff teaches that this reaction mixture is cycled *back and forth* between the *two* temperature regions shown. As submitted previously, it is noted that fig. 1 shows a TWO TEMPERATURE amplification process which lends itself to apparatus configurations that would *reciprocate* the reaction mixture rather than *recycling* it.

Onischenko provides a supporting disclosure that teaches methods for the continuous amplification of nucleic acids (col. 2-3, for example). Specifically, Onischenko teaches an apparatus for continuous nucleic acid amplification (fig. 1, for example) comprising: a continuous loop of tubing (fig. 1; tubes 1,2,3,4, for example) that recirculates an amplification reaction mixture through the appropriate temperatures required for amplification (col. 5, line 40-col. 6, line 5, for example), e.g. a denaturation temperature, followed by a annealing temperature, followed by an extension temperature, followed by another denaturing temperature, etc.

Thus, as previously submitted, in a THREE TEMPERATURE amplification process, which is clearly envisioned by Haff (col. 9, lines 30-35, for example), one of ordinary skill in the art at the time of invention would have known, as demonstrated in Onishenko, that the reaction mixture is to be moved successively through temperatures causing DENATURING, ANNEALING, EXTENSION, then back to DENATURING to start another cycle of amplification. One of ordinary skill in the art at the time of invention would have recognized, as demonstrated in Onishenko, that it is counter-productive and contrary to well known scientific methodology to flow a reaction mixture from the EXTENSION temperature back to the ANNEALING temperature. Thus, the

creation of an --endless-- recirculation path flows naturally from the teachings of Haff and Onishenko.

With regard to newly submitted amendments in Applicant's submission dated February 28, 2007 which require an inlet end an outlet end of the recirculation-path immersed within said reaction mixture tank, it is first noted that the right end of the tubing within the apparatus of fig.1 of Haff (number 22), i.e. the inlet, would necessarily have to be immersed in a PCR medium within a structure capable of holding such medium, i.e. a tank, in order for the pump to transfer such medium into the reaction system. Furthermore, it is submitted that one of ordinary skill in the art at the time of invention would have known, as demonstrated by Onishenko, that the PCR mixture, within in a THREE TEMPRATURE system, requires several circulation cycles to effectively amplify a PCR sample. Thus, it is submitted that one of ordinary skill in the art at the time of invention would have been motivated to, in a THREE TEMPERATURE as suggested by Haff and Onishenko, immerse the left end of the tubing within the apparatus of fig.1 of Haff (number 22), i.e. the outlet, within the same "tank" as the inlet, instead of a separate "tank", to effectively amplify a PCR sample through several cycles.

Furthermore, the teachings of Onishenko highlight that a "closed-loop" system is preferred since the system is simplified and heating of the PCR mixture can occur in a uniform manner (col. 3, line 40-col. 4, line15, for example). Thus, it is submitted that it is submitted that one of ordinary skill in the art at the time of invention would have been motivated to, in a THREE TEMPERATURE as suggested by Haff and Onishenko,

immerse the left end of the tubing within the apparatus of fig.1 of Haff (number 22), i.e. the outlet, within the same "tank" as the inlet, instead of a separate "tank", to allow for a simplified "closed-loop" system.

Thus, it would have been *prima facie obvious* to a practitioner of ordinary skill in the art at the time of invention to amplify a PCR sample by the way of a single path and reaction mixture tank as required by the current invention through the apparatus of fig. 1 since Haff and well known scientific methodology as demonstrated by Haff, suggests such a modification to continuously amplify the same reaction mixture through multiple amplification cycles in a simplified reaction system, thus arriving at the claimed invention.

Conclusion

Claim(s) 4, 6, 7, and 9-12 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

4/17/07

Christopher M. Babic
Patent Examiner
AU 1637

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

4/30/07